AMENDMENTS TO THE SPECIFICATION

Please amend paragraph [069] as the follow:

[069] In a preferred embodiment, with many or all of the AI algorithms, a fitness function is used to select between alternative members of the solution set to find the optimum solution. The fitness function is used to direct the evolution of the model (e.g. the pseudochromosome when a GA is used) and to allow non-deterministic methods to converge. In general, the fitness function may consist of several parts. In one embodiment, the fitness function may include a strict life/death decision based on validated pathways taken from the literature. That is, global solutions may be known to contain or avoid certain physiological unit operations or parameters, or dictate or preclude different temporal orders. For example, a membrane transport step may be known to be required, and thus any possible solutions which do not contain this physiological unit operation are eliminated. Similarly, certain enzymatic steps must be in certain orders: the enzymatic conversion of a substrate cannot come before its creation, etc. These "rules" are generally drawn from the literature or thermodynamic principles. "Constraints-based" modeling approaches, such as those described by [Proc. National Acad Sci. (USA) 95:4193-4198, 1998; Biotechnology Progress, 15:296, 1999; J. theor. Biol., 203:229-249, 2000] can be incorporated in the fitness function. However, it is also possible to create these "per se" rules, run the system and evaluate the output. For example, when it is not known whether a membrane transport function is involved, running the system with either rule and fitting it to the known empirical data can help elucidate the model. In another embodiment, the fitness function may be a goodness of fit measure to empirical data, e.g. the OMICS expressional genomic, proteomic, and metabolomic data already generated. At a simplistic level the fitness function can be considered as a statistical goodness of fit measurement in a curve fit to experimental data. In another embodiment, the fitness function may include user-definable limiting assumptions, such as a test for multiplicity of steady-states or violation of physical and chemical laws (i.e. ~~constrants~~ constraints). It can be argued that multiple steady-states (i.e., more than one possible physiological state being possible for a fixed set of growth conditions) are inefficient, like futile cycles, and would have been selected against in nature. In a preferred embodiment the fitness function includes more than one or all of the above described embodiments.